BioChem

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Editorial

Feature Papers in *BioChem*

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1. Introduction and Scope

Biochemistry, or the chemistry of life, is an interdisciplinary science that uses strategies and methods from all exact and natural sciences. In that sense, Biochemistry is a discipline known to be challenging for students, typically due to the extent and complexity of the content [1]. However, in the last 10 years, at least fifteen Nobel Prizes in Chemistry, Physiology and Medicine have been awarded in the field and/or for applications of Biochemistry, which reflects the importance of this area of knowledge in contemporary societies [2–7]. Biochemistry connects essential metal ions such as Mg^{2+}, Ca^{2+}, Na^{+} and Fe^{2+}, and organic compounds, such as nucleic acids, sugars, lipids and proteins, to make biological systems possible, representing a unique platform for interdisciplinary collaborations in teaching and in research [8,9]. Moreover, in addition to biomolecules (proteins, nucleic acids, sugars and lipids), small molecules are necessary for cellular homeostasis, for example, carbonate ions and phosphate ions, responsible for stabilizing physiological pH (close to 7.0) or antioxidants that prevent the effects of cellular stress, as well as due to environmental pollutants, such as metals and/or microplastics [10–12].

Biochemistry, as it is an interdisciplinary science, is very dynamic, and its boundaries are very hard to define not only because they are constantly changing but also because they are dependent on the specificities of each time period and scientific environments. Nevertheless understanding life on earth and human health are everlasting topics in biochemistry. Thus, this Special Issue titled "Feature Papers in *BioChem*" is expected to showcase interdisciplinary research in the diverse and interconnected fields of molecular biology, cell biology, structural biology, nucleic acid biology, chemical biology, synthetic biology, disease biology, biophysics, metallomics (or inorganic biochemistry) and theoretical biochemistry.

This Special Issue included six articles and four reviews. Among the articles, a wide range of topics were addressed, including our understanding of otolith proteomics in Atlantic cod [13], juvenile idiopathic arthritis' impact on long-term fertility due to prolonged exposure to immunosuppressive therapies [14], the role of tricyclic isoquinoline derivatives as antibacterial agents [15], the production of aromatic compounds in *Pseudomonas putida* [16], hydrogels made with Tilapia fish skin to increase collagen production [17], and the use of N-Myristoyltransferase inhibitors (NMTi) as a novel antiviral strategy against mammarenaviruses [18]. Additionally, the four reviews papers described the role of oxidative stress in the pathogenesis of the most common gastrointestinal diseases [19], the biotechnological production of vanillin [20], non-steroidal anti-inflammatory drugs' (NSAIDs) effects in the elderly population [21] and the biochemical mechanisms and applications of multiple cysteine-based protein ligases [22]. In fact, these ten contributions represent very good examples of the wide range of biochemistry boundaries identified in the 21 century. So far (4 June 2025), these 10 contributions have gathered 5 citations

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and 16,576 views, indicating an average of 1658 views per publication. Note that all these contributions have been published after June 2024, with six published in 2025 alone.

2. Contributions

The first paper published in the present Special Issue (SI) is entitled "Proteomic Blueprint of Atlantic Cod (Gadus morhua) Otoliths Revealing Environmental Stress Insights through Label-Free Quantitative Shotgun Proteomics" [13]. The study states that most identified proteins deposited daily and influenced by the environment are not implicated in the biomineralization of otolith [13]. It highlights the potential for the otolith proteome to recreate details of fish life history at previously unrealized levels. This contribution from Professor Banoub and collaborators is a very good example of how the boundaries of biochemistry can be promoted and interact simultaneously through the work of very different departments/faculties and research institutes in Canada, namely, for biochemistry, the Fisheries Centre and, for medicine, the Institute of Research in Cancer and Chemistry. Professor Banoub's research group and its collaborators also carried out research about the environmental impact of bioplastic use [23]. The second paper published in the present Special Issue is entitled "Anti-Müllerian Hormone Serum Levels as Biomarker of Ovarian Reserve in Adult Women with Juvenile Idiopathic Arthritis Treated with csDMARDs and/or bDMARDs: A Pilot Study" [14], conducted by the research group of Professor Elisa Gremese from the Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy. Professor Gremese was also involved in "The Gemelli Against COVID-19 Post-Acute Care Study Group" project, which described the importance of using an interdisciplinary approach coordinated by a geriatrician to manage the potential post-acute care needs of recovered COVID-19 patients [24]. Herein, it was suggested that ovarian reserve, as assessed by anti-Müllerian hormone serum levels, appears to be comparable between those with juvenile idiopathic arthritis and age-matched controls and does not appear to be influenced by disease characteristics or prior/concomitant exposure to immunosuppressive drugs.

The third review paper published in the present Special Issue is entitled "Synthesis and Investigation of Tricyclic Isoquinoline Derivatives as Antibacterial Agents" [15], conducted by the research group of Professor Andrew McDonagh from the University of Technology Sydney, Australia. In this paper, a series of six isoquinoline-based compounds were synthesized for developing broad-spectrum antibacterial compounds. The authors pointed out that although the compounds presented antibacterial properties, their cytotoxic properties against mammalian cell lines revealed some cytotoxic effects, suggesting limitations in their antibacterial applications without further development. Professor Andrew McDonagh's recent research interests have included studies of coumarin compounds for use as *Chlamydial* protease inhibitors and anti-chlamydial agents [25]. From Professor Caroline Ranquet of BGene Genetics, Grenoble, France, we received the publication entitled "Overproduction of Phenolic Compounds in *Pseudomonas putida* KT2440 Through Endogen Deregulation of the Shikimate Pathway" [16]. The introduction of specific engineered enzymes into a metabolically engineered *Pseudomonas putida* strain resulted in significantly increased production of p-coumaric acid. Recent collaborations involving Caroline Ranquet included research about the Fis family members that synergistically control the virulence of *Legionella pneumophila* [26]. Herein, through computational modeling and experimental validation, the authors identified specific amino-acid residues responsible for tyrosine-mediated feedback inhibition. By using targeted mutagenesis, the introduction of engineered 3-deoxy-D-arabino-heptulosonate 7-phosphate synthase (DAHP synthase) variants reduced the sensitivity to feedback inhibition [16].

Burns are the most common type of injury in everyday life, and wound healing presents several challenges and concerns in medicine. The studies from the research group

of Professor Ozge Cevik, School of Medicine, Aydin Adnan Menderes University, Turkey, about hydrogels made with Tilapia fish (TL, *Oreochromis niloticus*) skin show an increase in collagen production in burn treatment [17]. TL or TL-alginate hydrogels (AGTL) were applied to a burn wound created in Sprague–Dawley rats for 7 and 14 days, and the levels of hydroxyproline, a critical element in tissue reorganization, along with the gene expression levels of COL1A1, COL3A1, MMP-2 and MMP-9 and the protein expression levels of the matrix metalloproteinases (MMPs) MMP-2 and MMP-9, were evaluated. It was suggested that biological substances in the TL structure, in conjunction with alginate, were effective in the healing and reorganization of the wound tissue [20]. From the same group, studies on the anticarcinogenic properties of green-synthesized zinc oxide nanoparticles (ZnONPs) synthesized employing fresh *Citrus aurantium* aqueous extract on human breast cancer cells (MDA-MB-231) were described [27].

The sixth paper contributed by Professor Juan de la Torre, The Scripps Research Institute, La Jolla, USA, proposed a model of the effect of the NMT inhibitor on mammarenavirus cell entry and budding. NMT isozymes facilitate the addition of myristic acid to the glycines of stable signal peptides (SSPs) and Z proteins, protecting them from proteasome-mediated degradation. The viral glycoprotein precursor (GPC) is co- and post-translationally processed to produce a stable signal peptide (SSP), and the mature GP1 and GP2 subunits, together with the SSP, form the spikes that decorate the virus surface and mediate cell entry via receptor-mediated endocytosis. Myristoylated SSP interacts with GP2 to facilitate the fusion event in the late endosome required to complete the virus cell entry process, whereas myristoylated Z directs the virus assembly and budding process. The inhibition of SSP and Z myristoylation by NMT inhibitors results in the proteasome-mediated degradation of SSP and Z, which results in the inhibition of virus multiplication [18]. From the same authors, studies about repurposing drugs for synergistic combination therapies to counteract monkeypox virus tecovirimat resistance have been submitted [28].

The eighth contribution was a review article titled "Oxidative Stress-Induced Gastrointestinal Diseases: Biology and Nanomedicines—A Review" [19] from Dra Maryam Rezvani, the University of Cagliari, Italy. In this review, it was revealed that although oxidative stress in each part of the digestive system manifests itself in a specific way, all these diseases arise from the imbalance between the generation of the reactive intermediates (especially reactive oxygen species) and the antioxidant defense system. It was further pointed out that the annual incidence and mortality statistics of gastrointestinal diseases worldwide emphasize an urgent need to find an effective and non-invasive treatment method to overcome these life-threatening problems. Another review paper entitled "Biotechnological Advances in Vanillin Production: From Natural Vanilla to Metabolic Engineering Platforms" [20] was conducted by the research group of Professor Isabel Desgagne-Penix, Université du Québec à Trois-Rivières, Canada. The review highlights the significance of vanillin in various markets, its diverse applications and the current state of bio-engineered production using both prokaryotic and eukaryotic biological systems. The authors aim was to provide a current and innovative overview of vanillin bioengineering across various host systems, with special consideration given to microalgae. Altogether, the use of these systems to support the biotechnological production of vanillin, while leveraging the photosynthetic capabilities of microalgae to capture CO_2 and convert it into biomass, can significantly reduce the overall carbon footprint [20]. A recent study from Professor Isabel Desgagne-Penix's research group discusses the potential of norbelladine derivatives for use in Alzheimer's disease research and for future pharmaceutical developments in the field [29].

Professor Hugo Ribeiro, the Faculty of Medicine, the University of Porto, Portugal, as well as several Health Units, submitted a systematic review entitled "Appropriate Prescription of Non-Steroidal Anti-Inflammatory Drugs in Geriatric Patients—A Systematic

Review" [21]. This study aimed to evaluate the cardiovascular, gastrointestinal and renal safety profiles of ibuprofen, naproxen, acemetacin, diclofenac, celecoxib and etoricoxib in elderly patients. From the 2086 articles identified, twenty studies analyzed cardiovascular (CV) safety, fourteen analyzed gastrointestinal (GI) safety, and four analyzed renal safety. When CV risk is the main concern, celecoxib or naproxen are a good first choice. In high-GI-risk groups, the combination of proton pump inhibitor (PPI) with naproxen or celecoxib use is recommended. When renal function is the focus, celecoxib remains the first line of therapy. Diclofenac use in elderly populations should be avoided. Celecoxib is a good choice for elderly patients for whom it is difficult to direct pain treatment based on a single known risk factor [21].

Last but not the least, from the Purdue University, USA, we received a review paper describing protein ligases as nature's gift to the field of protein synthesis and engineering. The generation of active proteins via recombinant expression or chemical total synthesis has limitations in terms of yield and functionality. However, nature has provided a solution to this problem through evolving protein ligases that catalyze the formation of amide bonds between peptides/proteins, which can be exploited by protein engineers to develop robust functional proteins [22]. Several biochemical mechanisms and applications of multiple cysteine-based protein ligases have been identified, such as sortase A, an transpeptidase enzyme; butelase-1, an asparaginyl endopeptidase; OaAEP1, similar to butelase-1; trans-glutaminase 2, a member of the transglutaminase protein family; E3 ligases; and inteins, believed to act as self-catalyzing enzymes able to undergo *cis*- or *trans*-splicing. When comparing the mechanism of intein splicing with that of native chemical ligation (NCL), the authors found many similarities, which suggest that nature inspired the design of this chemical ligation [22]. From the same research group, led by Professor Qingfei Zheng, a study about transglutaminase 2-mediated histone monoaminylation and its role in cancer was received [30].

3. Biochemistry Insights Across Diverse Scientific Fields

In this Special Issue, a total of 50 authors from 8 countries (France, Australia, Canada, Italy, Iran, Turkey, Portugal, and the USA) were involved, with the large majority being young researchers, thus pointing out the presence of a new generation of scientists in several biochemistry fields. Altogether, this Special Issue reflects, in the 21 century, the existence of distinct and emergent biochemical contributions crossing several biochemical boundaries and applications.

Overall, five interdisciplinary aspects of biochemistry insights can be highlighted in this Special Issue (Figure 1):

1. The Cod Otolith Study [13] and Anti-Müllerian Hormone (AMH) Research [14] both use proteins as biomarkers. The otolith proteome reflects environmental stress and life history, while AMH serves as a biomarker for ovarian reserve. These studies highlight biochemistry's role in translating molecular signatures (proteins/hormones) into diagnostic or ecological insights. The benefits of further making use of natural biomaterials are best illustrated by the fact that hydrogels made with Tilapia fish can be used to treat burn wounds [17].
2. *Pseudomonas putida* phenolic overproduction [16] and vanillin bioengineering [20] focus on manipulating metabolic pathways. Both use enzyme engineering to optimize yields of high-value compounds (p-coumaric acid, vanillin). These studies exemplify biochemistry's role in sustainable bioproduction.
3. The Isoquinoline Antibacterial [15] and Non-Steroidal Anti-Inflammatory Drugs Safety [21] Reviews address the biochemical challenge of balancing efficacy and safety.

In the study of burn wound treatment [17], natural biomaterials could safe sources of hydrogels.

4. Oxidative Stress in Gastrointestinal Diseases [19] and Phenolic Compound Production [16] intersect through reactive oxygen species (ROS) and antioxidants. Phenolics (like p-coumaric acid) are natural antioxidants, suggesting potential applications in mitigating oxidative stress-related gastrointestinal diseases. This finding aligns with the review's call for non-invasive treatments, possibly via nanomedicine or engineered antioxidants.
5. DAHP Synthase Engineering [16] conducts enzyme modulation by reducing feedback inhibition to boost phenolic synthesis. These studies highlight biochemistry's role in enzyme kinetics and inhibitor design for industrial/therapeutic applications (Figure 1). Related to the inhibitor design, the inhibitor of NMT isozymes, which is required for the myristoylation of SSP, can stop virus multiplication [18]. Biochemistry reveals nature's mechanism and helps us to learn from nature to improve protein engineering, such as by using cysteine-based protein ligases and intein splicing [22].

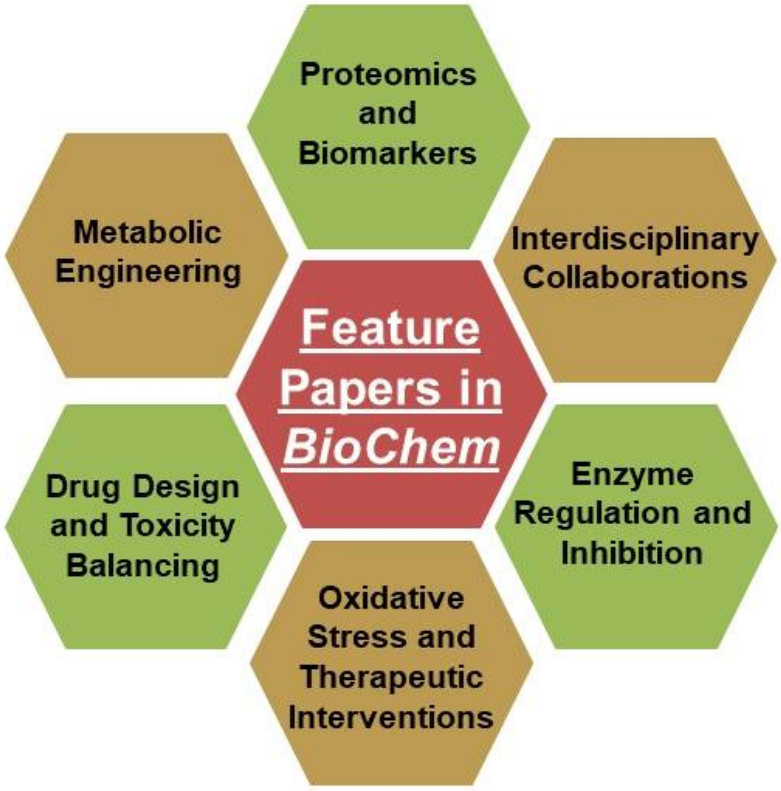

Figure 1. Feature papers in *BioChem*: Topics related to biochemistry boundaries.

This collection of Special Issue papers collectively illustrate biochemistry's central role in addressing global challenges—environmental monitoring, sustainable production, drug development and health diagnostics (Figure 1). The papers emphasize the interplay between molecular mechanisms, translational applications and interdisciplinary collaboration, showcasing biochemistry as a dynamic field at the boundary between life sciences, medicine and sustainability. Allegorically, biochemistry represents a key cog in the "clock of the knowledge", dynamically joining several scientific fields, such as chemistry, biology and medicine, among others, for perfect shared innovation and development (Figure 2).

Figure 2. Biochemistry represents a key cog in the "clock of the knowledge", dynamically joining several scientific wheels such as chemistry, biology and medicine, among others, for achieving perfect shared innovation and development.

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